REMARKS

Claims 1-8, 11-12, 22 and 25-29 are currently under consideration. Claim 12 was objected to by the Examiner in view of a typographical error in the second line. Claim 12 is amended herein to correct the error. The amendment does not add new matter. Applicants note that although previously withdrawn, Claims 13-21 and 30-33 had not been cancelled. Claims 13-21 and 30-33 are cancelled herewith

Claim Rejections under 35 U.S.C. §103(a)

Claims 1-8, 11-12, 22, and 25-29 stand rejected under 103(a) over Tartaglia et al. (US Patent 5,972,621, "Tartaglia") in view of Harlow et al. (Antibodies, A Laboratory Manual, Cold Spring Harbor (1998); "Harlow").

The Claims of the present application are directed to a method of identifying an agonist WSX receptor antibody with a particular binding affinity. Claim 1 recites not only producing one or more agonist antibodies which specifically bind to the extracellular domain of a receptor having a WSX motif comprising the extracellular domain sequence within SEQ ID NO:2, but also selecting an agonist antibody so produced that binds to the extracellular domain with a Kd of no more than about 1×10^{-7} M.

Thus, Claim 1 of the current application is not simply directed to methods of producing antibodies. Rather, it is directed to a method of identifying those antibodies that bind to and activate receptors with a particular extracellular domain sequence (agonist antibodies). Claim 1 is further directed to a sub-species of these agonist antibodies, since they must bind with a Kd of no more than about $1X10^{-7}$M. The dependent claims are directed to further subsets of these elements.

In rejecting the claims, the Examiner asserts that Tartaglia teaches a method of identifying antibodies which decrease body weight in animals by specifically binding to the extracellular domain of Ob receptor. In support of his position, the Examiner refers to particular portions of the text of Tartaglia including column 5, lines 44-60, column 6, lines 50-5, and column 8, lines 22-25. Applicants respectfully disagree and submit that contrary to the Examiner's position, there is no disclosure in Tartaglia that teaches or suggests antibodies which decrease body weight in animals, and there is no disclosure that teaches or suggests a method of

identifying an agonist WSX receptor antibody as claimed. As discussed in detail below, none of the sections referred to by the Examiner, or any other disclosure in Tartaglia for that matter, teaches or suggests a method of identifying agonist antibodies that bind to and activate Ob receptor.

With respect to column 5, lines 44-60, Tartaglia provides a list of things that are encompassed by his invention. These include, for example, agonists and antagonists of ObR, antibodies, antisense molecules and transgenic animals. As the list includes transgenic animals and molecules that act on gene expression, it is clear that it is not a list of various types of agonists and antagonists. Thus, while this section of Tartaglia contains the term "antibodies," it does not teach or suggest agonist antibodies that bind to and activate Ob receptor.

Similarly, the Abstract mentions antibodies to the Ob receptor but does not teach or suggest agonist antibodies. Col. 6, lines 50-55 refers to the extracellular domain of Ob receptor, but has no teaching or suggestion of antibodies, much less of agonist antibodies. Col. 8, lines 22-25 also refers to functional domains of the Ob receptor, such as the ECD, but has no disclosure of antibodies.

Tartaglia discusses antibodies to the Ob receptor generally at columns 22-23. However, this disclosure concerns production of antibodies that are used to detect Ob receptor in a sample, antibodies that are used to evaluate the effect of compounds on expression of Ob receptor, antibodies that are used in conjunction with gene therapy to evaluate Ob receptor expression and antibodies that are used to *inhibit* abnormal Ob receptor activity (column 22, lines 25-42). There is no teaching or suggestion of antibodies that *activate* Ob receptor.

Harlow discloses that antibodies with certain affinities are useful for immunoprecipitation and other immunoassays. Harlow has no disclosure regarding agonist antibodies. Nevertheless, the Examiner concludes that in view of the disclosures in Tartaglia and Harlow, one of skill in the art would be motivated to not only produce agonist antibodies, but also to select agonist antibodies with a Kd of no more than about 1×10^{-7} M, as claimed. Applicants strongly disagree and submit that in the *absence of any teachings regarding agonist antibodies*, such a combination would not lead one of skill in the art to arrive at the claimed invention.

Even if Tartaglia were to be found to somehow suggest agonist antibodies to the Ob receptor, which Applicants maintain it does not, the Examiner has failed to make a prima facie case of obviousness, as outlined below.

The Examiner has Failed to Make a Prima Facie Case of Obviousness

Section 2143 of the M.P.E.P. summarizes the three requirements that must be established for a prima facie case of obviousness:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As none of the three requirements for a §103 rejection have been met in the present rejection, Applicants submit that the Examiner has not made a prima facie case of obviousness

There is no motivation to combine the teachings of Tartaglia with the teachings of Howard.

First, there is no motivation within Tartaglia or Harlow to create the combination that the Examiner has suggested (creating an agonist antibody with a particular minimum Kd). There is no teaching in Tartaglia that an agonist antibody should have any particular affinity, much less that an agonist antibody should have the same affinity as an antibody used for immunoassays. An affinity that may be useful for one process, such as immunoprecipitation, is not necessarily useful for an unrelated and much more complicated process such as activation of a receptor by binding of a functional agonist antibody. One skilled in the art would recognize that a range of Kds that is useful for the process of immunoblotting, as taught by Harlow, is of no particular relevance to a desirable Kd for binding in an agonistic manner.

The idea that antibodies with different affinities are desirable for different purposes is supported by Harlow, which actually teaches different affinities for different uses. In particular, the affinity for cell staining provided in Harlow is 10^6 mol^{-1} to 10^8 mol^{-1} and the affinity for immunoblotting is 10^6 mol^{-1} to 10^8 mol^{-1}. Indeed, of the ranges described, only one, immunoprecipitation, has a range that could be arguably described as possibly close to 10^7 mol^{-1}.

Thus, in making the present rejection, the Examiner is actually picking one of the three ranges to combine with Tartaglia. However, there is *no teaching that any of those ranges are the desirable range for agonist antibodies*. Indeed, if Harlow teaches or suggests anything, it is that there are different ranges for each of an antibody's different uses.

Tartaglia has no teaching or suggestion that a desirable range of affinities for agonist antibodies is the same as for antibodies to be used for immunoassays as disclosed in Harlow. Since the useful range of affinities depends upon the context of the use, and Harlow does not address the relevant range of affinities of agonistic antibodies, it is clear that there would be no motivation, to one of skill in the art, to combine the teachings of Tartaglia and Harlow in the manner described by the Examiner.

There is no reasonable expectation of success based on the references.

Second, there is no reasonable expectation of success that a combination of Tartaglia and Harlow would succeed without the disclosure of the present application.

Agonist antibodies act as ligands for the receptor. Thus, the requirements for such antibodies are much different than for antibodies that must simply recognize the receptor. As a result, methods for making agonist antibodies are not enabled by disclosure relating to the production of antibodies for other purposes. Tartaglia contains only a passing reference to antibodies as agonists. Tartaglia does *not* disclose the actual production of an agonist antibody and provides no teaching of how to make an agonist antibody. Moreover, Tartaglia never suggests producing and selecting any antibody, much less an agonist antibody, with a Kd of no more than about $1x10^{-7}$M. Thus, based on the disclosure in Tartaglia one of skill in the art would not have a reasonable expectation of success in producing an agonist antibody and selecting an agonist antibody so produced with a particular binding affinity.

Harlow does nothing to overcome the deficiencies in Tartaglia. Harlow only establishes that a particular range of Kds is typical for certain types of limited antibody associations, i.e. binding for immunoprecipitation. Further, Harlow teaches that one cannot simply transfer preferred binding affinities to various uses of antibodies. Thus, Harlow has no disclosure that is relevant to the production and selection of agonist antibodies.

As neither of the cited references provide any teachings regarding making an agonist antibody and selecting an agonist antibody with a particular affinity as claimed, there can be no expectation of success in the combination proposed by the Examiner.

Not all of the elements are taught in the references.

Finally, the combination of references does not teach all of the elements of the claims.

As defined in the present specification, an agonist antibody is "...an antibody which is able to activate native sequence WSX receptor. The agonist antibody of particular interest herein is one which mimics one or more (e.g. all) of the biological properties of naturally occurring WSX ligand, OB protein." (p 20, lines 27-33 of Application as filed). Thus, an agonist antibody is not merely characterized as an antibody that can bind to a target, but by its *activation* of the receptor. As is well known in the art, not all antibodies are agonist antibodies. As a result, disclosure of antibodies generally does not teach or suggest agonist antibodies.

Tartaglia does not teach or suggest how to make an agonist antibody and does not teach or suggest selecting an agonist antibody with a particular affinity.

These deficiencies are not made up for by Harlow. Harlow has no teaching regarding agonist antibodies, but rather, merely discusses antibodies for use in particular immunological techniques. The antibodies used in those techniques do not have to possess the particular activities of the agonist antibodies and thus are not equivalent. There is no teaching that a particular affinity is universally beneficially for antibodies, much less of any desirable affinity for agonist antibodies.

In view of the lack of a motivation to combine the Tartaglia and Harlow references, the lack of an expectation of success in such a combination and the lack of the necessary teachings, Applicants submit that the Examiner has failed to make a prima facie case of obviousness. Thus, the Applicants respectfully request that the present rejection of Claim 1 be withdrawn. All of the remaining claims depend from Claim 1, and contain all of the features thereof with additional distinguishing features. Thus, the rejection of Claims 2-8, 11,12, 22 and 25-29 should be withdrawn as well.

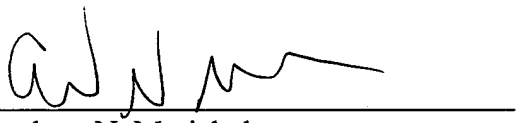
Conclusion

For the reasons set forth above, it is respectfully submitted that the present Application is in condition for allowance. Should any issues remain, the Examiner is invited to contact the Applicants' representative at the telephone number appearing below in order to resolve such issues promptly.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: March 29, 2004

By: 

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